

AMENDMENTS TO THE CLAIMS

Please amend claims 7 and 24-26 and add new claims 32-34, as shown in the following listing of claims, which will replace all prior versions and listings of claims in the application. Claims 6-34 are pending in the application. Claims 20-21 were withdrawn without prejudice in response to a restriction requirement.

In the claims:

1. – 5. (canceled)

6 (previously presented). An isolated nucleic acid molecule which comprises a nucleotide sequence encoding a variable region of a non-human TCR α or β peptide wherein said TCR is human HLA-restricted and specific for a tumor-associated antigen, the variable region of the non-human TCR α or β peptide being directly coupled to a transmembrane and cytoplasmic region of a CD3, CD8 or CD16 receptor.

7 (currently amended). The nucleic acid molecule of ~~claim~~ claim 6 wherein the transmembrane and cytoplasmic region is the ζ region of CD3.

8 (previously presented). The nucleic acid molecule of claim 7 wherein said ζ region is that of human CD3.

9 (previously presented). The nucleic acid molecule of claim 6 wherein said non-human TCR is murine.

10 (original). The nucleic acid molecule of claim 6 wherein said nucleotide sequence encodes a single-chain TCR.

11 (previously presented). The nucleic acid molecule of claim 10 wherein said single-chain TCR consists of the variable α region fused to variable β region by a flexible linker and said β region is fused to a transmembrane and cytoplasmic region of a CD3, CD8 or CD16 receptor.

12 (previously presented). The nucleic acid molecule of claim 11 wherein said flexible linker is of the formula $(\text{Gly}_4\text{Ser})_3$ (SEQ ID NO: 65).

13 (previously presented). The nucleic acid molecule of claim 11 wherein said region is ζ of CD3.

14 (previously presented). The nucleic acid molecule of claim 13 wherein the chain is derived from human CD3.

15 (original). A recombinant expression system which expression system comprises the nucleotide sequence of claim 6 operatively linked to control sequences for effecting its expression in a host cell.

16 (original). A recombinant host cell modified to contain the expression system of claim 15.

17 (original). The recombinant cells of claim 16 which are T cells.

18 (original). A method to obtain cells which display TCR or a functional derivative thereof at their surface, said TCR or derivative being human HLA-restricted and specific for a tumor-associated antigen, which method comprises culturing the cells of claim 16 under

conditions wherein said nucleotide sequence is expressed and said TCR or derivative is displayed at the surface.

19 (original). Recombinant cells displaying a TCR receptor or derivative thereof at their surface wherein said TCR or derivative is human HLA-restricted and specific for a tumor-associated antigen prepared by the method of claim 18.

20 (withdrawn). A method to identify antigens associated with a tumor which method comprises contacting said tumor or a fraction thereof with the cells of claim 19 under conditions wherein said tumor or fraction is lysed only if said tumor displays the TAA for which said TCR or derivative is specific.

21 (withdrawn). A method to effect treatment of a tumor in a human, wherein said tumor is characterized by a specific tumor-associated antigen (TAA) which method comprises administering to said human subject peripheral blood cells from said subject which have been modified to contain an expression system for a nucleotide sequence which encodes a TCR or derivative thereof which is human HLA-restricted and specific for said TAA.

22 (previously presented). The isolated nucleic acid molecule of claim 6, wherein the tumor-associated antigen is Her2/neu, ras, p53, tyranase, MART, Gp100, MAGE, BAGE, or MUC-1.

23 (previously presented). The isolated nucleic acid molecule of claim 6, wherein the encoded non-human TCR is restricted to HLA A1, A2, A3 or B7.

24 (currently amended). The isolated nucleic acid molecule of claim 6, wherein the encoded TCR comprises covalently linked in sequence: 1) a non-human TCR α or β peptide;

and 2) a transmembrane and cytoplasmic region of a CD3 receptor as shown between nucleotide numbers 927 to 1334 of ~~Figure 3A-B~~ Figures 3A-3D.

25 (currently amended). The isolated nucleic acid molecule of claim 10, wherein the encoded single-chain TCR comprises covalently linked in sequence: 1) a non-human TCR α peptide; 2) a flexible linker; 3) a non-human TCR β peptide; and 4) a transmembrane and cytoplasmic region of a CD3 receptor as shown between nucleotide numbers 927 to 1334 of ~~Figure 3A-B~~ Figures 3A-3D.

26 (currently amended). The isolated nucleic acid molecule of claim 24 or 25 further comprising a CD8 hinge as shown between nucleotide numbers 786 to 914 of ~~Figure 3A-B~~ Figures 3A-3D.

27 (previously presented). The isolated nucleic acid molecule of claim 26, wherein the CD8 hinge is directly coupled between the non-human β peptide and the transmembrane and cytoplasmic region of the CD3 receptor.

28 (previously presented). The isolated nucleic acid of claim 6, wherein the CD3, CD8, or CD16 receptor is human.

29 (previously presented). An expression vector comprising the isolated nucleic acid of claim 6.

30 (previously presented). The expression vector of claim 28 further comprising sequence encoding a leader sequence.

31 (previously presented). An isolated nucleic acid molecule which comprises a nucleotide sequence encoding a variable region of a non-human TCR α or β peptide wherein said TCR is human HLA-restricted and specific for a tumor-associated antigen.

32 (new). An isolated nucleic acid molecule which comprises a nucleotide sequence encoding a variable region of a non-human TCR α or β peptide wherein said TCR is human HLA-restricted and specific for a tumor-associated antigen, the variable region of the non-human TCR α or β peptide being coupled to a transmembrane and cytoplasmic region of a CD3, CD8 or CD16 receptor, wherein the transmembrane and cytoplasmic region is the ζ region of a CD3, CD8, or CD16 receptor, and further comprising a polypeptide spacer between the TCR variable domain and the transmembrane and cytoplasmic region of a CD3, CD8, or CD16 receptor.

33 (new). The nucleic acid molecule of claim 6 wherein said nucleotide sequence encodes a single-chain TCR.

34 (new). An isolated nucleic acid molecule which comprises a nucleotide sequence encoding a single-chain T-cell receptor (TCR) comprising a variable region of a non-human TCR α chain fused to a variable region of a non-human TCR β chain, said TCR α and TCR β chains comprising a non-human TCR, wherein the single-chain TCR is specific for a tumor-associated antigen (TAA) and restricted by human HLA.